REMARKS

I. Status of Claims.

Claims 1-7 and 9-15 are pending.

Claims 1-2, 6 and 10-13 are amended in a manner that is believed to overcome rejections contained in the pending Office Action. Support for these amendments can be found throughout the drawings, specification and claims as originally filed. No new matter or issues are believed to be introduced by these amendments.

II. Rejection of claims 1-7 and 9-15 under 35 USC 112, first paragraph.

In the Office Action dated May 6, 2005, the Examiner rejected claims 1-7 and 9-15 under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention.

A. Examiner's rejection: The Examiner stated that the rejected claims are drawn to a method for modulating behavioral and neurological adaptive responsiveness to stress by applying to the central nervous system a therapeutically effective amount of an inhibitor of the DP IV enzyme. The Examiner further stated that "Applicant specifically points out that the limitation "applying to the central nervous system" is what distinguishes the instant invention from the prior art of record. Thus, it appears that one of the distinguishing inventive concepts of the instant invention is one of the specific methods of application of inhibitors of DP IV to central nervous system. However, the instant specification , as filed fails to provide any guidance on how to apply inhibitors of DP IV exclusively to central nervous system with omission of the rest of the body when these inhibitors are applied by inhalation or suppository".

B. Applicants' Claimed Invention: Applicants' claimed invention as set forth in amended claims 1 and 2 from which the other rejected claims depend, is directed to the "treatment of anxiety". by inhibition of DP IV within the central nervous system. As shown in examples 3 and 4 of the instant disclosure, Applicants' invention is directed to the beneficial neurological effects that result from the inhibition of DP IV within the central nervous system by "introducing into the central nervous system a therapeutically effective amount of an inhibitor of dipeptidyl peptidase IV" alone or in combination with NPY (claim 5). The outstanding and

unexpected beneficial effect of this combination is shown in particular in examples 3 and 4. Applicants have furthered amended claims 6 and 10-13 to emphasize that the introduction into the central nervous system of DP IV inhibitors can be accomplished via parenteral introduction, e.g. i.c.v. administration. Applicants submit that the claims as amended are more than enabled by the instant disclosure and respectfully request this rejection be withdrawn.

IV. Rejection of claims 2, 7 and 10 under 35 USC 102(b).

The Examiner rejected claims 2, 7 and 10 stand rejected under 35 USC 102(b) as being anticipated by Powers et al. (WO 95/29691, 1995, Document BL, IDS of Paper No. 2) ("Powers"). Applicants respectfully traverse this rejection.

A. Examiner's Rejection: The Examiner' rejection stated that Powers discloses administration of inhibitors of dipeptidyl peptidase IV and such administration leads to the decrease of enzymatic activity of DP IV and consequently to reduction of degradation of its natural endogenous substrate. The Examiner stated that the instant claims, as written, encompass application of DP IV inhibitors to the central nervous system by inhalation or suppository, which appears to be not limited to the application of the inhibitors exclusively to central nervous system. The Examiner further stated that because the claims are broadly drawn to methods of administration of inhibitors of DP IV Powers fully meets the limitations of the instant claims.

B. Applicants' Claimed Invention: Applicants' claimed invention as described in amended claim 2, from which claims 7 and 10 depend, is directed to the "treatment of anxiety" as a central nervous system disorders. Applicants claimed method of treating central nervous system disorders such as anxiety is by the "introducing into the central nervous system" DP IV-inhibitors.

C. Disclosure of Powers: Power discloses the use of peptidyl derivative of diesters of α-aminoalkylphosphonic acids, particularly those with proline or related structures, their use in inhibiting serine proteases with chymotrypsin-like, elastase-like, and dipeptidyl peptidase IV specificity. The disclosure of Powers is restricted to the use of DP IV-inhibitors as anti-inflammatory agents, anticoagulants, anti-tumor agents, and anti-AIDS agents. Powers neither discloses applying DP IV inhibitors to the "central nervous system" nor the treatment of anxiety.

D. Deficiencies of Powers: Claim 2 as amended, from which rejected claims 7 and 10 depend, is directed to the "treatment of anxiety" as a central nervous system disorders. Unlike Applicants' claimed invention, Powers is completely devoid of any disclosure of the use of DP IV-inhibitors for the treatment of central nervous system disorders. Contrary to Applicants' disclosure, Powers is also devoid of any teaching of "introducing into the central nervous system a therapeutically effective amount of a DP IV-inhibitors", as Applicants have disclosed and claimed. Nor does Powers disclose the use of DP IV-inhibitors within the central nervous system that are introduced via parenteral route as set forth in amended claim 10. Given Applicants' claimed method of introducing into the central nervous system DP IV-inhibitors and the absence of an anticipatory teaching in Powers, Applicants respectfully suggest that in view of the above and the amended claims, this 102 rejection is unsupported and request that this rejection be withdrawn.

VII Rejection of claims 1, 3-4, 6, 9, 11-12 and 14 under 35 USC 102(b).

The Examiner rejected claims 1, 3-4, 6, 9, 11-12 and 14 under 35 USC 102(b) as being anticipated by Powers et al. (WO 95/29691, 1995, Document BL, IDS of Paper No. 2) ("Powers").

A. Examiner's Rejection: The Examiner's rejection stated that Powers discloses inhibitors of dipeptidyl peptidase IV and their use of administration as anti-inflammatory agents, anticoagulants, anti-tumor agents and anti-AIDS agents. Administration of a therapeutic amount of inhibitors of Powers leads to the decrease of enzymatic activity of DP IV and consequently to the reduction of degradation of its natural endogenous substrate. As such, the Examiner reasoned, the administration of DP IV-inhibitors as disclosed by Powers leads to reduction in stress responsiveness and anxiety.

B. Applicants' Claimed Invention: Applicants' claimed invention as set forth in amended claims 1 or 2 from which the other rejected claims depend, is directed to the "treatment of anxiety." Applicants' claimed invention is directed to the beneficial neurological and psychophysiological effects that result from the inhibition of DP IV within the central nervous system by "introducing into the central nervous system a therapeutically effective amount of an inhibitor of dipeptidyl peptidase IV" (emphasis added to highlight newly amended language).

Furthermore, as shown in examples 3 and 4, Applicants' invention is directed to the beneficial and unexpected neurological effects that result from the inhibition of DP IV within the central nervous system by "introducing into the central nervous system a therapeutically effective amount of an inhibitor of dipeptidyl peptidase IV" alone or in combination with NPY (see claim 5). The outstanding beneficial effect of this combination is shown in particular in examples 3 and 4.

C. Disclosure of Powers: Powers discloses the use of peptidyl derivative of diesters of α-aminoalkylphosphonic acids, particularly those with proline or related structures, their use in inhibiting serine proteases with chymotrypsin-like, elastase-like, and dipeptidyl peptidase IV specificity and their roles as anti-inflammatory agents, anticoagulants, anti-tumor agents, and anti-AIDS agents. Powers does not disclose, however, "introducing into the central nervous system a therapeutically effective amount of an inhibitor of dipeptidyl peptidase IV."

D. Deficiencies of Cited References: Unlike Applicants' claimed invention, as amended, Powers does not disclose the "treatment of anxiety" resulting from central nervous system disorders using an inhibitor of DP IV, which specific disclosure is required to support a 102(b) rejection. Neither does Powers disclose the treatment of anxiety by "introducing into the central nervous system a therapeutically effective amount of an inhibitor of dipeptidyl peptidase" alone or in combination with NPY. It is made clear throughout the description of the present invention that the therapeutic targets of the present invention are the receptors of neuropeptides. The main target is the neuropeptide Y and subsequently its receptor Y1. These receptors are localized in the central nervous system (e.g. brain) of mammals. As it is known in the art, the central nervous system is a separate compartment of the body/organism of mammals, which is strongly demarcated from the rest of the body by the so called "blood-brain-barrier." Accordingly, the claims of the present invention specify inhibition of dipeptidyl peptidase IV (DP IV) activity in this compartment by "introducing into the central nervous system a therapeutically effective amount of an inhibitor of dipeptidyl peptidase IV" in order to reach the desired pharmaceutical target. Powers does not disclose "introducing into the central nervous system a therapeutically effective amount of a competitive inhibitor of the dipeptidyl peptidase

IV (DP IV)" as Applicants have disclosed and claimed. The inhibition of DP IV per the teachings of Powers does not occur within the central nervous system.

As has been clearly enunciated by the Federal Circuit: Anticipation requires the presence in a single prior art reference the disclosure of each and every element of the claimed invention, arranged as in the claim. Lindermann Maschinenfabrik GMBH v. American Hoist and Derrick Co., 221 USPQ 481, 485 (Fed Cir. 1984) (emphasis added). Here the requirement of showing each and every element of Applicant's claimed invention in a single prior art reference has not been met since Powers fails to disclose Applicants' claimed invention of introducing into the central nervous system DPIV inhibitors as detailed above. In light of these deficiencies in Powers, it is respectfully submitted that the 35 U.S.C. §102(b) is improper, may be properly withdrawn, and Applicants so request.

VII. Rejection of claims 1-4, 6, 7, and 14 under 35 USC 102(e).

The Examiner rejected claims 1-4, 6, 7, and 14 under 35 USC 102(e) as being anticipated by Demuth et al., U.S. Patent No. 6,319,893 (Demuth '893). Applicants respectfully traverse this rejection.

A. Examiner's Rejection: The Examiner stated that Demuth '893 describes the administration to a mammal of therapeutically effective amounts of an inhibitor of DP IV. The Examiner further stated that Demuth '893 also discloses methods of administration (parenterally, orally), pure forms of inhibitors, and formulations with physiologically acceptable adjuvants.

B. Applicants' Claimed Invention: Applicants' claimed invention as set forth in the amended claims is directed to the "treatment of anxiety" resulting from central nervous system disorders. The instant claims are directed to methods of treating these central nervous system disorders such as anxiety through the administration of DP IV-inhibitors by "introducing into the central nervous system a therapeutically effective amount of an inhibitor of dipeptidyl peptidase IV" alone or in combination with NPY.

C. Disclosure of Demuth '893: Demuth '893 discloses a method of raising the blood sugar level in a mammal having hypoglycemia. The method disclosed in Demuth '893 reduces degradation of glucagons by administering to the mammal a therapeutically effective amount of an inhibitor of dipeptidyl peptidase IV and physiologically acceptable adjuvants and/or excipients. Demuth '893 does not disclose introducing DP IV inhibitors to the central nervous

system as Applicants have disclosed and claimed. In particular, the use of DP IV-inhibitors within the central nervous system is not disclosed in Demuth. In contradiction, it is recognized by those skilled in the art that introduction into the central nervous system of a therapeutically effective compound, which is used for treating systemic diseases (such as for instance hypoglycemia) is to be avoided.

D. Deficiencies of Demuth '893: In fact, Demuth '893 is completely devoid of any disclosure related to DP IV-inhibitors for the treatment of central nervous system disorders. Demuth also discloses nothing regarding the use of DP IV-inhibitors by "introducing into the central nervous system a therapeutically effective amount of an inhibitor of dipeptidyl peptidase" either alone or in combination with NPY. Nowhere does Demuth mention NPY. The inhibition of DP IV within the teachings of Demuth '893 does not occur within the central nervous system. Applicants respectfully submit that Demuth simply can not support this rejection and therefore request that this rejection be withdrawn.

VIII. Rejection of claims 1-4, 6, 7, 9-12 and 14 under Obviousness-type Double Patenting.

A rejection was made to claims 1-4, 6, 7, 9-12 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,319,893 (Demuth '893). Applicants respectfully but vigorously suggest that the claimed subject matter of the rejected claims differ from that of the claims of Demuth '893, as discussed immediately above. Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

The claims remaining within the application are believed to patentably distinguish over the prior art and to be in condition for allowance. Early and favorable consideration of this application is respectfully requested.

Respectfully submitted,

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Dated: July 5, 2005